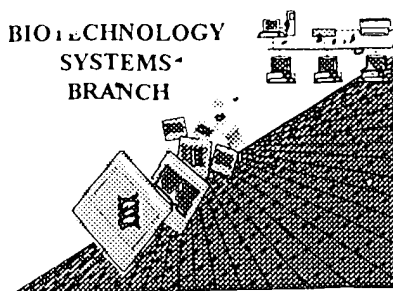


BEST AVAILABLE COPY

RAW SEQUENCE LISTING
ERROR REPORT

BIOLOGY
SYSTEMS
BRANCH



#6

BC

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/622613

Source: PCT

Date Processed by STIC: 08/30/2001

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.

PATENTIN 2.1 e-mail help: patin21help@uspto.gov or phone 703-306-4119 (R. Wax)

PATENTIN 3.0 e-mail help: patin3help@uspto.gov or phone 703-306-4119 (R. Wax)

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 3.0 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW:

Checker Version 3.0

The Checker Version 3.0 application is a state-of-the-art Windows based software program employing a logical and intuitive user-interface to check whether a sequence listing is in compliance with format and content rules. Checker Version 3.0 works for sequence listings generated for the original version of 37 CFR §§1.821 - 1.825 effective October 1, 1990 (old rules) and the revised version (new rules) effective July 1, 1998 as well as World Intellectual Property Organization (WIPO) Standard ST.25.

Checker Version 3.0 replaces the previous DOS-based version of Checker, and is Y2K-compliant. Checker allows public users to check sequence listings in Computer Readable form (CRF) before submitting them to the United States Patent and Trademark Office (USPTO). Use of Checker prior to filing the sequence listing is expected to result in fewer errored sequence listings, thus saving time and money.

Checker Version 3.0 can be down loaded from the USPTO website at the following address:

<http://www.uspto.gov/web/offices/pac/checker>

Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: 09/622613
ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE		
1 <input type="checkbox"/> Wrapped Nucleics Wrapped Aminos	The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."	
2 <input type="checkbox"/> Invalid Line Length	The rules require that a line not exceed 72 characters in length. This includes white spaces.	
3 <input type="checkbox"/> Misaligned Amino Numbering	The numbering under each 5 th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.	
4 <input type="checkbox"/> Non-ASCII	The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.	
5 <input type="checkbox"/> Variable Length	Sequence(s) _____ contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.	
6 <input type="checkbox"/> PatentIn 2.0 "bug"	A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.	
7 <input type="checkbox"/> Skipped Sequences (OLD RULES)	Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence: (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.	
8 <input type="checkbox"/> Skipped Sequences (NEW RULES)	Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence. <210> sequence id number <400> sequence id number 000	
9 <input type="checkbox"/> Use of n's or Xaa's (NEW RULES)	Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.	
10 <input type="checkbox"/> Invalid <213> Response	Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence	
11 <input checked="" type="checkbox"/> Use of <220>	Sequence(s) _____ missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)	
12 <input type="checkbox"/> PatentIn 2.0 "bug"	Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.	
13 <input type="checkbox"/> Misuse of n	n can only be used to represent a single nucleotide in a nucleic acid sequence. N is not used to represent any value not specifically a nucleotide.	

AMC/MH - Biotechnology Systems Branch - 08/21/2001

The type of errors shown exist throughout the Sequence Listing. Please check subsequent sequences for similar errors.

PCT09

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/622,613

DATE: 08/30/2001

TIME: 06:44:30

Input Set : A:\Nih343-1.app

Output Set: N:\CRF3\08302001\I622613.raw

Does Not Comply
Corrected Diskette Needed

p 4 of 7

The type of errors shown exist throughout
the Sequence Listing. Please check subsequent
sequences for similar errors.

```

3 <110> APPLICANT: Rybak, Susanna M.
4     Newton, Dianne L.
5     The United States of America
6     as represented by The Secretary of the
7     Department of Health and Human Services
9 <120> TITLE OF INVENTION: Recombinant Anti-Tumor RNase
11 <130> FILE REFERENCE: 015280-343100US
13 <140> CURRENT APPLICATION NUMBER: US 09/622,613
14 <141> CURRENT FILING DATE: 2000-08-17
16 <150> PRIOR APPLICATION NUMBER: US 60/079,751
17 <151> PRIOR FILING DATE: 1998-03-27
19 <150> PRIOR APPLICATION NUMBER: WO PCT/US99/06641
20 <151> PRIOR FILING DATE: 1999-03-26
22 <160> NUMBER OF SEQ ID NOS: 43
24 <170> SOFTWARE: PatentIn Ver. 2.0
26 <210> SEQ ID NO: 1
27 <211> LENGTH: 312
28 <212> TYPE: DNA
29 <213> ORGANISM: Rana pipiens
31 <220> FEATURE:
32 <221> NAME/KEY: CDS
33 <222> LOCATION: (1)..(312)
34 <223> OTHER INFORMATION: ribonuclease (RaPLR1)
36 <400> SEQUENCE: 1
37 caa gac tgg ctt acg ttt cag aag aag cac ctg aca aac acc cgg gat   48
38 Gln Asp Trp Leu Thr Phe Gln Lys Lys His Leu Thr Asn Thr Arg Asp
39   1           5           10           15
41 gtt gac tgt aat att atc atg tca aca aac ttg ttc cac tgc aag gac   96
42 Val Asp Cys Asn Ile Ile Met Ser Thr Asn Leu Phe His Cys Lys Asp
43           20           25           30
45 aag aac act ttt atc tat tca cgt cct gag cca gtg aag gcc atc tgt   144
46 Lys Asn Thr Phe Ile Tyr Ser Arg Pro Glu Pro Val Lys Ala Ile Cys
47           35           40           45
49 aaa gga att ata gcc tcc aaa aat gtg tta act acc tct gag ttt tat   192
50 Lys Gly Ile Ile Ala Ser Lys Asn Val Leu Thr Thr Ser Glu Phe Tyr
51   50           55           60
53 ctc tct gat tgc aat gta aca agc agg cct tgc aag tat aaa tta aag   240
54 Leu Ser Asp Cys Asn Val Thr Ser Arg Pro Cys Lys Tyr Lys Leu Lys
55  65           70           75           80
57 aaa tca act aat aca ttt tgt gta act tgt gag aat caa gct cca gta   288
58 Lys Ser Thr Asn Thr Phe Cys Val Thr Cys Glu Asn Gln Ala Pro Val
59           85           90           95
61 cat ttc gtg ggt gtc gga cat tgc   312
62 His Phe Val Gly Val Gly His Cys
63   100
66 <210> SEQ ID NO: 2
67 <211> LENGTH: 104

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RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/622,613

DATE: 08/30/2001

TIME: 06:44:30

Input Set : A:\Nih343-1.app

Output Set: N:\CRF3\08302001\I622613.raw

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68 <212> TYPE: PRT
69 <213> ORGANISM: Rana pipiens
71 <400> SEQUENCE: 2
72 Gln Asp Trp Leu Thr Phe Gln Lys Lys His Leu Thr Asn Thr Arg Asp
73   1           5           10           15
75 Val Asp Cys Asn Ile Ile Met Ser Thr Asn Leu Phe His Cys Lys Asp
76           20           25           30
78 Lys Asn Thr Phe Ile Tyr Ser Arg Pro Glu Pro Val Lys Ala Ile Cys
79           35           40           45
81 Lys Gly Ile Ile Ala Ser Lys Asn Val Leu Thr Thr Ser Glu Phe Tyr
82           50           55           60
84 Leu Ser Asp Cys Asn Val Thr Ser Arg Pro Cys Lys Tyr Lys Leu Lys
85  65           70           75           80
87 Lys Ser Thr Asn Thr Phe Cys Val Thr Cys Glu Asn Gln Ala Pro Val
88           85           90           95
90 His Phe Val Gly Val Gly His Cys
91           100
94 <210> SEQ ID NO: 3
95 <211> LENGTH: 312
96 <212> TYPE: DNA
97 <213> ORGANISM: Artificial Sequence
99 <220> FEATURE:
100 <223> OTHER INFORMATION: Description of Artificial Sequence:Rana pipiens
101     ribonuclease with Met23Leu substitution
102     (recombinant RaPLR1 Met23Leu)
104 <220> FEATURE:
105 <221> NAME/KEY: CDS
106 <222> LOCATION: (1)..(312)
107 <223> OTHER INFORMATION: RaPLR1 Met23Leu
109 <400> SEQUENCE: 3
110 caa gac tgg ctt acg ttt cag aag aag cac ctg aca aac acc cgg gat      48
111 Gln Asp Trp Leu Thr Phe Gln Lys Lys His Leu Thr Asn Thr Arg Asp
112   1           5           10           15
114 gtt gac tgt aat aat atc ctg tca aca aac ttg ttc cac tgc aag gac      96
115 Val Asp Cys Asn Ile Leu Ser Thr Asn Leu Phe His Cys Lys Asp
116           20           25           30
118 aag aac act ttt atc tat tca cgt cct gag cca gtg aag gcc atc tgt      144
119 Lys Asn Thr Phe Ile Tyr Ser Arg Pro Glu Pro Val Lys Ala Ile Cys
120           35           40           45
122 aaa gga att ata gcc tcc aaa aat gtg tta act acc ttt gag ttt tat      192
123 Lys Gly Ile Ile Ala Ser Lys Asn Val Leu Thr Thr Phe Glu Phe Tyr
124           50           55           60
126 ctc tct gat tgc aat gta aca agc agg cct tgc aag tat aaa tta aag      240
127 Leu Ser Asp Cys Asn Val Thr Ser Arg Pro Cys Lys Tyr Lys Leu Lys
128  65           70           75           80
130 aaa tca act aat aca ttt tgt gta act tgt gag aat caa gct cca gta      288
131 Lys Ser Thr Asn Thr Phe Cys Val Thr Cys Glu Asn Gln Ala Pro Val
132           85           90           95
134 cat ttc gtg ggt gtc gga cat tgc      312

```

RAW SEQUENCE LISTING

DATE: 08/30/2001

PATENT APPLICATION: US/09/622,613

TIME: 06:44:30

Input Set : A:\Nih343-1.app

Output Set: N:\CRF3\08302001\I622613.raw

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135 His Phe Val Gly Val Gly His Cys
136                               100
139 <210> SEQ ID NO: 4
140 <211> LENGTH: 104
141 <212> TYPE: PRT
142 <213> ORGANISM: Artificial Sequence
W--> 144 <220> FEATURE:
W--> 144 <223> OTHER INFORMATION:
144 <400> SEQUENCE: 4
145 Gln Asp Trp Leu Thr Phe Gln Lys Lys His Leu Thr Asn Thr Arg Asp
146   1                               5                               10                               15
148 Val Asp Cys Asn Asn Ile Leu Ser Thr Asn Leu Phe His Cys Lys Asp
149                               20                               25                               30
151 Lys Asn Thr Phe Ile Tyr Ser Arg Pro Glu Pro Val Lys Ala Ile Cys
152   35                               40                               45
154 Lys Gly Ile Ile Ala Ser Lys Asn Val Leu Thr Thr Phe Glu Phe Tyr
155   50                               55                               60
157 Leu Ser Asp Cys Asn Val Thr Ser Arg Pro Cys Lys Tyr Lys Leu Lys
158   65                               70                               75                               80
160 Lys Ser Thr Asn Thr Phe Cys Val Thr Cys Glu Asn Gln Ala Pro Val
161                               85                               90                               95
163 His Phe Val Gly Val Gly His Cys
164                               100
167 <210> SEQ ID NO: 5
168 <211> LENGTH: 315
169 <212> TYPE: DNA
170 <213> ORGANISM: Artificial Sequence
172 <220> FEATURE:
173 <223> OTHER INFORMATION: Description of Artificial Sequence:Rana pipiens
174     ribonuclease with Met at position 1 (recombinant
175     Met(-1) RaPLR1)
177 <220> FEATURE:
178 <221> NAME/KEY: CDS
179 <222> LOCATION: (1)..(315)
180 <223> OTHER INFORMATION: Met(-1) RaPLR1
182 <400> SEQUENCE: 5
183 atg caa gac tgg ctt acg ttt cag aag aag cac ctg aca aac acc cgg      48
184 Met Gln Asp Trp Leu Thr Phe Gln Lys Lys His Leu Thr Asn Thr Arg
185   1                               5                               10                               15
187 gat gtt gac tgt aat aat atc atg tca aca aac ttg ttc cac tgc aag      96
188 Asp Val Asp Cys Asn Asn Ile Met Ser Thr Asn Leu Phe His Cys Lys
189                               20                               25                               30
191 gac aag aac act ttt atc tat tca cgt cct gag cca gtg aag gcc atc      144
192 Asp Lys Asn Thr Phe Ile Tyr Ser Arg Pro Glu Pro Val Lys Ala Ile
193   35                               40                               45
195 tgt aaa gga att ata gcc tcc aaa aat gtg tta act acc tct gag ttt      192
196 Cys Lys Gly Ile Ile Ala Ser Lys Asn Val Leu Thr Thr Ser Glu Phe
197   50                               55                               60
199 tat ctc tct gat tgc aat gta aca agc agg cct tgc aag tat aaa tta      240

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RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/622,613

DATE: 08/30/2001

TIME: 06:44:30

Input Set : A:\Nih343-1.app

Output Set: N:\CRF3\08302001\I622613.raw

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200 Tyr Leu Ser Asp Cys Asn Val Thr Ser Arg Pro Cys Lys Tyr Lys Leu
201 65 70 75 80
203 aag aaa tca act aat aca ttt tgt gta act tgt gag aat caa gct cca 288
204 Lys Lys Ser Thr Asn Thr Phe Cys Val Thr Cys Glu Asn Gln Ala Pro
205 85 90 95
207 gta cat ttc gtg ggt gtc gga cat tgc 315
208 Val His Phe Val Gly Val Gly His Cys
209 100 105

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212 <210> SEQ ID NO: 6

213 <211> LENGTH: 105

214 <212> TYPE: PRT

215 <213> ORGANISM: Artificial Sequence

W--> 217 <220> FEATURE:

W--> 217 <223> OTHER INFORMATION:

217 <400> SEQUENCE: 6

218 Met Gln Asp Trp Leu Thr Phe Gln Lys Lys His Leu Thr Asn Thr Arg

219 1 5 10 15

221 Asp Val Asp Cys Asn Asn Ile Met Ser Thr Asn Leu Phe His Cys Lys

222 20 25 30

224 Asp Lys Asn Thr Phe Ile Tyr Ser Arg Pro Glu Pro Val Lys Ala Ile

225 35 40 45

227 Cys Lys Gly Ile Ile Ala Ser Lys Asn Val Leu Thr Thr Ser Glu Phe

228 50 55 60

230 Tyr Leu Ser Asp Cys Asn Val Thr Ser Arg Pro Cys Lys Tyr Lys Leu

231 65 70 75 80

233 Lys Lys Ser Thr Asn Thr Phe Cys Val Thr Cys Glu Asn Gln Ala Pro

234 85 90 95

236 Val His Phe Val Gly Val Gly His Cys

237 100 105

240 <210> SEQ ID NO: 7

241 <211> LENGTH: 315

242 <212> TYPE: DNA

243 <213> ORGANISM: Artificial Sequence

245 <220> FEATURE:

246 <223> OTHER INFORMATION: Description of Artificial Sequence: Rana pipiens

247 ribonuclease with Met at position 1 and Met24Leu

248 substitution (recombinant Met(-1) RaPLR1 Met23Leu)

250 <220> FEATURE:

251 <221> NAME/KEY: CDS

252 <222> LOCATION: (1)..(315)

253 <223> OTHER INFORMATION: Met(-1) RaPLR1 Met23Leu

255 <400> SEQUENCE: 7

256 atg caa gac tgg ctt acg ttt cag aag aag cac ctg aca aac acc cgg 48

257 Met Gln Asp Trp Leu Thr Phe Gln Lys Lys His Leu Thr Asn Thr Arg

258 1 5 10 15

260 gat gtt gac tgt aat aat atc ctg tca aca aac ttg ttc cac tgc aag 96

261 Asp Val Asp Cys Asn Asn Ile Leu Ser Thr Asn Leu Phe His Cys Lys

262 20 25 30

264 gac aag aac act ttt atc tat tca cgt cct gag cca gtg aag gcc atc 144

A 213 response of "Artificial Sequence" requires an explanation or description in field 223.

Errored

The type of errors shown exist throughout the Sequence Listing. Please check subsequent sequences for similar errors.

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/622,613

DATE: 08/30/2001

TIME: 06:44:30

Input Set : A:\Nih343-1.app

Output Set: N:\CRF3\08302001\I622613.raw

```

265 Asp Lys Asn Thr Phe Ile Tyr Ser Arg Pro Glu Pro Val Lys Ala Ile
266          35          40          45
268 tgt aaa gga att ata gcc tcc aaa aat gtg tta act acc ttt gag ttt 192
269 Cys Lys Gly Ile Ile Ala Ser Lys Asn Val Leu Thr Thr Phe Glu Phe
270          50          55          60
272 tat ctc tct gat tgc aat gta aca agc agg cct tgc aag tat aaa tta 240
273 Tyr Leu Ser Asp Cys Asn Val Thr Ser Arg Pro Cys Lys Tyr Lys Leu
274 65          70          75          80
276 aag aaa tca act att aca ttt tgt gta act tgt gag aat caa gct cca 288
277 Lys Lys Ser Thr Ile Thr Phe Cys Val Thr Cys Glu Asn Gln Ala Pro
278          85          90          95
280 gta cat ttc gtg ggt gtc gga cat tgc 315
281 Val His Phe Val Gly Val Gly His Cys
282          100          105

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285 <210> SEQ ID NO: 8

286 <211> LENGTH: 105

287 <212> TYPE: PRT

288 <213> ORGANISM: Artificial Sequence

W--> 290 <220> FEATURE:

W--> 290 <223> OTHER INFORMATION: *Errored*

290 <400> SEQUENCE: 8

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291 Met Gln Asp Trp Leu Thr Phe Gln Lys Lys His Leu Thr Asn Thr Arg
292 1          5          10          15
294 Asp Val Asp Cys Asn Asn Ile Leu Ser Thr Asn Leu Phe His Cys Lys
295          20          25          30
297 Asp Lys Asn Thr Phe Ile Tyr Ser Arg Pro Glu Pro Val Lys Ala Ile
298          35          40          45
300 Cys Lys Gly Ile Ile Ala Ser Lys Asn Val Leu Thr Thr Phe Glu Phe
301          50          55          60
303 Tyr Leu Ser Asp Cys Asn Val Thr Ser Arg Pro Cys Lys Tyr Lys Leu
304 65          70          75          80
306 Lys Lys Ser Thr Ile Thr Phe Cys Val Thr Cys Glu Asn Gln Ala Pro
307          85          90          95
309 Val His Phe Val Gly Val Gly His Cys
310          100          105

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313 <210> SEQ ID NO: 9

314 <211> LENGTH: 111

315 <212> TYPE: PRT

316 <213> ORGANISM: Artificial Sequence

318 <220> FEATURE:

319 <223> OTHER INFORMATION: Description of Artificial Sequence: Rana pipiens

320 ribonuclease with (His)6 tag, Met at position 7

321 and Met30Leu substitution (recombinant Met(-1)

322 RaPLR1 Met23Leu-(His)6)

324 <400> SEQUENCE: 9

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325 His His His His His His Met Gln Asp Trp Leu Thr Phe Gln Lys Lys
326 1          5          10          15
328 His Leu Thr Asn Thr Arg Asp Val Asp Cys Asn Asn Ile Leu Ser Thr
329          20          25          30

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VERIFICATION SUMMARY

PATENT APPLICATION: US/09/622,613

DATE: 08/30/2001

TIME: 06:44:31

Input Set : A:\Nih343-1.app

Output Set: N:\CRF3\08302001\I622613.raw

L:144 M:258 W: Mandatory Feature missing, <220> FEATURE:
L:144 M:258 W: Mandatory Feature missing, <223> OTHER INFORMATION: *Proceed*
L:217 M:258 W: Mandatory Feature missing, <220> FEATURE:
L:217 M:258 W: Mandatory Feature missing, <223> OTHER INFORMATION:
L:290 M:258 W: Mandatory Feature missing, <220> FEATURE:
L:290 M:258 W: Mandatory Feature missing, <223> OTHER INFORMATION:
L:397 M:258 W: Mandatory Feature missing, <220> FEATURE:
L:397 M:258 W: Mandatory Feature missing, <223> OTHER INFORMATION:
L:470 M:258 W: Mandatory Feature missing, <220> FEATURE:
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L:874 M:258 W: Mandatory Feature missing, <220> FEATURE:
L:874 M:258 W: Mandatory Feature missing, <223> OTHER INFORMATION:
L:947 M:258 W: Mandatory Feature missing, <220> FEATURE:
L:947 M:258 W: Mandatory Feature missing, <223> OTHER INFORMATION: